Mitogen activated protein kinases SakA (HOG1) and MpkC collaborate for *Aspergillus fumigatus* virulence.

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Abstract

Here, we investigated which stress responses were influenced by the MpkC and SakA mitogen-activated protein kinases of the high-osmolarity glycerol (HOG) pathway in the fungal pathogen *Aspergillus fumigatus*. The ΔsakA and the double ΔmpkC ΔsakA mutants were more sensitive to osmotic and oxidative stresses, and to cell wall damaging agents. Both MpkC::GFP and SakA::GFP translocated to the nucleus upon osmotic stress and cell wall damage, with SakA::GFP showing a quicker response. The phosphorylation state of MpkA was determined post exposure to high concentrations of congo red and Sorbitol. In the wild-type strain, MpkA phosphorylation levels progressively increased in both treatments. In contrast, the ΔsakA mutant had reduced MpkA phosphorylation, and surprisingly, the double ΔmpkC ΔsakA had no detectable MpkA phosphorylation. A. fumigatus ΔsakA and ΔmpkC were virulent in mouse survival experiments, but they had a 40% reduction in fungal burden. In contrast, the ΔmpkC ΔsakA double mutant showed highly attenuated virulence, with approximately 50% mice surviving and a 75% reduction in fungal

burden. We propose that both cell wall integrity (CWI) and HOG pathways collaborate, and that MpkC could act by modulating SakA activity upon exposure to several types of stresses and during CW biosynthesis.

Beteiligte Forschungseinheiten

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